Title & Detailed Synopsis of the Proposed Ph.D. Thesis

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DEVELOPMENT OF GREEN-INSPIRED SYNTHETIC PROTOCOLS FOR BIOLOGICALLY RELEVANT MOLECULAR HYBRIDS

a) Origin of the research problem

Among a number of green parameters in designing synthetic methods for organic molecules, to maintain energy-efficiency during any transformation is now regarded as a key one so as to reduce the utilization of fossil-fuels. Use of these fossil fuels as the conventional energy sources is one of the major causes toward environmental pollutions with all kinds of subsequent outcomes. Thus, to minimizing energy usage in chemical transformations can be regarded as a way-out for the protection of our environment and its sustainability. During large-scale industrial production, energy usage is really a vital concern. So, if we can cut-down energy consumption anyway or can make use of renewable non-conventional energy sources in our processes, it would contribute a lot to our endeavors in protecting our environment and its sustainability, no doubt!

The use of high temperature in synthesis when necessary us is understandable in order to obtain the desired molecule. By not accepting that synthetic methods have to be run at high temperatures and can be done at ambient conditions, is an important step toward along the path of continuous improvement. It is to keep in mind that so much of the most elegant chemistry, the most complex chemistry, the most important chemistry, is carried out by ***Nature*** at ambient temperatures. To ignore ***Nature*** as our most important chemistry teacher, mentor, and inspiration is unwise at best, and harmful and futile at worst. With this view, the present investigator feels very much excitement to take-up the challenge in designing room temperature-based synthetic protocols for the synthesis of some biologically relevant molecular hybrids. In addition, other aspects of green credentials would also be considered.

A Molecular hybrid is regarded as a new molecular entity developed via the process of molecular hybridization (MH) — a strategy analogous to conventional combination therapy with the expectation that the two drugs are covalently linked and available as a single entity. Hence, a molecular hybrid is anticipated to possess some sorts of extended biological profile. A fruitful synthetic hybrid composite may have the ability to

interact with more than one receptor, and thus triggers more than one biological response. This spectacular field has now created a stir among the synthetic and medicinal chemistry at large, and they have taken the dominating challenge in designing and synthesizing such hybrid molecular scaffolds to boost the ongoing development in present drug discovery programmes.

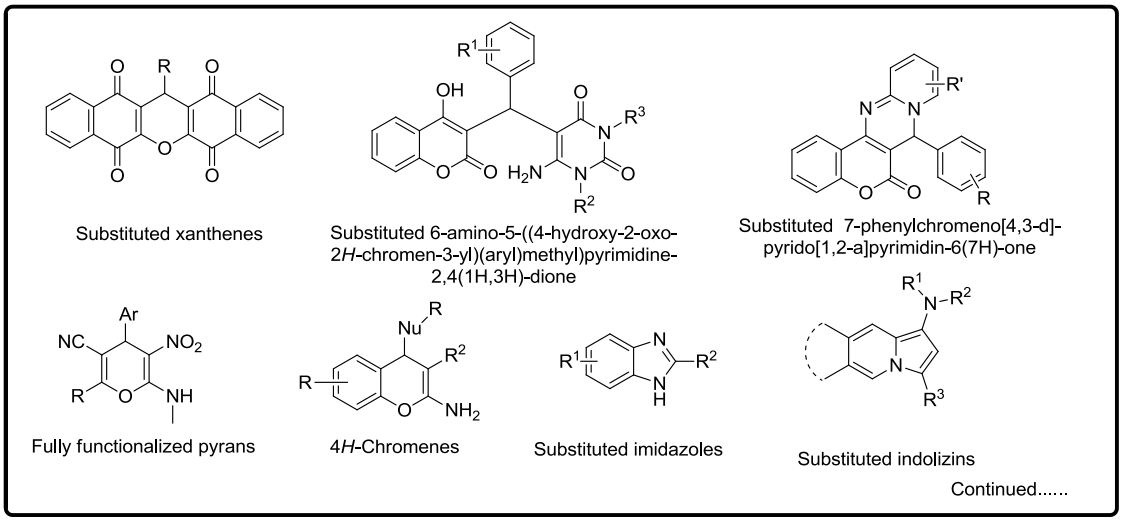
Under this demanding scientific platform, the present investigator is proposing to take the dedicated challenge to attain energy-efficiency in performing a chemical reaction by judicious screening of reaction conditions capable to carry out the transformation only at ambient conditions (room temperature and pressure) so as to make good use of ***Nature's*** enormous source of spontaneous energy that eventually cut-down environmental pollutions as a whole, thereby generating new series of molecular hybrids of promising biological interest.

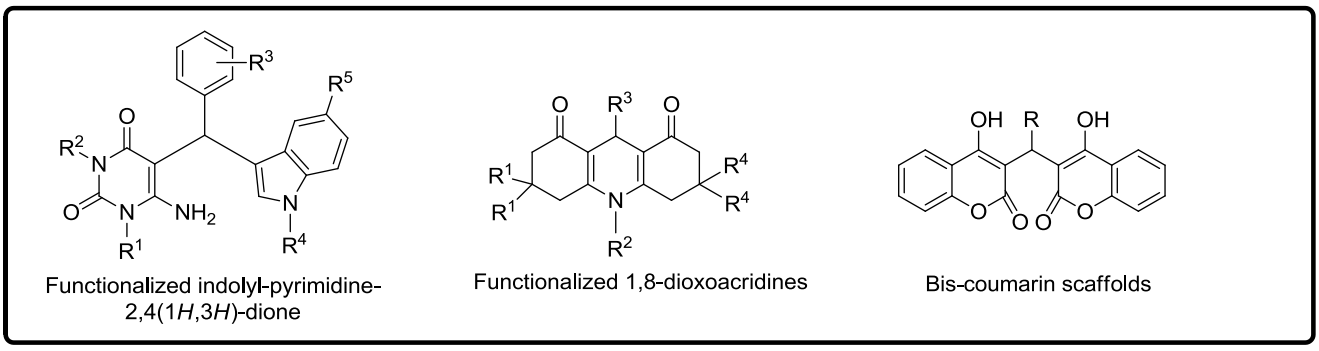
b) Objectives of the present work plan

- To develop eco-friendly MCR methodologies to achieve high atom-economy, avoiding multi-step complex processes either at room temperature and atmospheric pressure
- To perform synthesis of organic scaffolds under focused ultrasound irradiation at room temperature
- To perform synthesis of organic scaffolds using ball-milling technique
- To use nontoxic/less toxic and easily available chemicals as starting materials
- To use environmentally benign, cost-effective and easily available catalysts that could be recycled and reused
- To develop non-toxic or less toxic catalyst-systems
- To use water and/or aqua-organo mixture (e.g. water-ethanol) as solvent
- Easy purification of the final products avoiding chromatographic separation

Some targeted organic scaffolds of interests:

Some targeted molecular scaffolds are screened as part of the programme, and sketched below.





Scheme 1: Some targeted heterocyclic scaffolds of our interest

Point-wise summary of the major parts of the present work plan:

- Selection of targeted heterocyclic motif (**Scheme 1**) and designing its functionalized libraries
- Retroanalysis of the target motif and selection of cheap and commercially available substrates
- Designing for energy-efficient reaction protocols at room temperature
- Application of the newly developed protocol in synthesizing more complex libraries of interest

Planning to consider few more green chemistry parameters like:

- introduction of novel one-pot multicomponent technique
- to verify the reaction under catalyst-free condition
- use of efficient, non-toxic, commercially available, cheap catalyst
- use of solvent-free condition or to use suitable green solvents like water/ethanol/glycerol/PEG

c) General methodology to be followed

Simple experimental set-up is to be developed for one-pot syntheses of targeted heterocycles (**Scheme 1**). The substrates and the catalyst (or catalyst free condition) will be added in a reaction vial (at a time or in a sequential manner). If needed suitable solvent will be added into the reaction mixture. The reaction mixture will be stirred magnetically at room temperature. The progress of the reaction will be monitored by TLC/PMR. After completion, the reaction mixture will be settled down and the solvent will be removed under reduced pressure, and the residue will be purified simply by recrystallization and/or by column chromatographic technique. For characterization of the synthesized heterocycles, their detailed spectral studies including FT-IR, ^{1}H-NMR, ^{13}C-NMR, DEPT, HR-MS as well as elemental analyses will be performed. In certain cases, X-ray analysis of unit crystals as to be developed of the products will also be taken care of!

d) Future prospect

The research outcomes would embody a considerable amount of new works relating to the development of green methodologies for a number of novel biologically relevant heterocyclic compounds which would attract researchers from various multi-disciplinary fields for their further studies, particularly on the physio-chemical properties, in silico biological potentials, experimental (in vitro and in vivo) studies on their potential

pharmaceutical efficacies and also use of the protocols as developed for library synthesis of lead drug candidates.

e) References

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